REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 1-13 are pending in the present application. Claim 1 has been amended to more particularly point out and distinctly claim the present invention.

In the outstanding Official Action, claims 1 and 5-13 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-46 of U.S. Patent No. 5,871,921. Claims 2-4 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-46 of U.S. Patent No. 5,871,921 in view of URDEA et al. Applicant believes that the present amendment obviates these rejections.

A terminal disclaimer to U.S. Patent No. 5,871,921 is attached. It is believed that the terminal disclaimer overcomes these rejections. A copy of the Agreement on Assignment of Intellectual Property Rights of U.S. Patent No. 5,871,921 to Ulf LANDEGREN is enclosed along with the corresponding PTO-1595 form. As one can see, the assignment can be found at Reel 014446, Frame 0295.

In the outstanding Official Action, claims 1, 5, 6 and 9-13 were rejected under 35 USC §103(a) as allegedly being

obvious over NILSSON et al. in view of FILDES et al. This rejection is respectfully traversed.

Applicant respectfully submits that the proposed combination of NILSSON et al. in view of FILDES et al. fails to disclose or suggest the claimed invention.

In the claimed invention, a padlock probe is anchored to a solid phase, to which the nucleic acid sequence to be analyzed, is added. A detectable marker is linked to the padlock probe. This allows a detectable moiety to remain bound (see specification, page 2, line 26). The padlock probe also contains a cleavable segment. For a better understanding, the Examiner's attention is respectfully directed to Figure 1 which provides an example of this arrangement.

The nucleic acid-containing sample is added to the anchored probe and a segment of the nucleic acid sequence (the target sequence)is hybridized to the complementary end-segments of the padlock probe. As a result, the padlock probe becomes circularized through ligation of the ends. Those padlock probes which have not hybridized to a nucleic acid sequence are cleaved in a way that the detectable marker is removed together with the dissociable segment. These dissociable segments are removed by washing.

On the solid phase, the padlock probes, which have interacted with the nucleic acid sequence from the sample, can easily be detected through analysis of the detectable marker.

Since the nucleic acid sequence of interest is bound to the solid phase, the washing step is more easily performed and allows less dissolved markers to be present when the detection step is performed, thus resulting in noise reduction.

Upon reviewing the cited publications, applicant believes that neither NILSSON et al. nor FILDES et al. teach the detectable moiety that remains anchored to the solid phase.

In the NILSSON et al. publication, padlock probes are used for localization and detection of a specific segment of a single stranded DNA. A padlock probe, which is defined as an oligonucleotide probe for localized detection of specific nucleic acids composed of two target-complementary end-segments connected by a linker, is added to the solid phase anchored single-stranded DNA. The padlock probe, which is not provided with any cleavable function or dissociable detectable functions, is hybridized to and circularized on the segment of the single-stranded DNA of interest.

Contrary to the assertions of the Official Action, the non-ligated probes of Figure 4 are not removed by cleaving the probes (they do not contain a cleavable function). They are removed because they are not linked to the target sequence. Moreover, the probes do not contain a solid phase anchor. They become anchored to the probes only if they are ligated in a target sequence dependent manner. This nucleic acid sequence can

then be read by use of detectable markers linked to the padlock probe.

In an effort to remedy the deficiencies of NILSSON et al., the Official Action cites to FILDES et al. However, FILDES et al. disclose a process wherein the hybridization is carried out under conditions such that the sequence-specific oligonucleotide (SSO) probes bind to the nucleic acid to form stable hybrid duplexes only if the hybridizing region of each of the probes is exactly complementary to the nucleic acid. The hybrids formed between the nucleic acid and the SSO probes can then be detected. Thus, this invention teaches the same concept as the NILSSON et al. publication. Indeed, neither publication provides the necessary teaching and motivation to modify and combine their teachings to obtain the claimed invention.

Thus, in view of the above, applicant believes that the proposed combination of NILSSON et al. in view of FILDES et al. fails to render obvious claims 1, 5, 6 and 9-13.

Claims 2-4 were rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of FILDES et al. further in view of URDEA et al. Applicant believes that URDEA et al. fail to remedy the deficiencies of NILSSON et al. in view of FILDES et al. URDEA et al. do not disclose the possibility of letting a detectable moiety remain anchored on the solid phase as set forth in the claimed invention. Moreover, while the Official Action argues that the use of multimers

according to URDEA et al. would be used in order to improve the sensitivity of the methods, branched or bifurcated probes are not essential to the sensitivity of the claimed method. One of ordinary skill in the art would lack the motivation and necessary expectation of success to combine and modify the teachings of the publications to obtain the claimed invention.

Claims 7 and 8 were rejected under 35 USC §103(a) as allegedly being unpatentable over NILSSON et al. in view of FILDES et al. further in view of BIRKENMEYER et al. This rejection is respectfully traversed.

BIRKENMEYER et al. disclose a gap filling ligase chain reaction wherein the object of the method is to decrease the occurrence of target independent ligation (see column 2, lines 30-31). In the claimed invention, the probes are optionally designed to hybridize to the target molecule to leave a small gap between the adjacent probe ends (see specification, page 4, lines 29-31). As a result, applicant believes that the BIRKENMEYER et al. publication teaches away from the claimed invention.

Thus, applicant believes that the proposed combination of NILSSON et al. in view of FILDES et al. further in view of BIRKENMEYER et al. fails to render obvious claims 7 and 8.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 1-13, as presented.

Allowance and passage to issue on that basis are accordingly respectfully requested.

Please charge the terminal disclaimer fee of $110 to Deposit Account No. 25-0120.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

The Appendix includes the following items:

- a terminal disclaimer

- copy of Agreement on Assignment of Intellectual Property Rights of U.S. Patent No. 5,871,921

- PTO-1595 form of assignment of U.S. Patent No. 5,871,921